

of exo-3,6-epoxy-1,2,3,4-tetrahydrophthalic anhydride added in 10 drops of dimethyl formamide. The pH was maintained at 9.0 for 30 minutes. After 30 minutes the pH was dropped to 7.5 and the solution allowed to equilibrate for an additional 30 minutes. The neutral solution was centrifuged at 9,000 rpm for 20 minutes, the supernatant removed and pH adjusted to 4.3 to precipitate the neutral soluble, epoxy-modified collagen. The precipitate was washed three times with sterile water and reconstituted in 0.005M phosphate buffer, pH 8.6, containing 2% sterile glycerol. The resulting solution was clear, transparent and viscous. One aliquot of about 5 ml was removed and exposed to 254nm UV light for 5 minutes. The material thickened but did not polymerize to a hard film. Another aliquot of 5 ml was removed and 25 ul of sodium persulfate (20mg/ml) added. This was also exposed to 254 nm UV irradiation for 2 minutes. The material polymerized to a relatively firm, but flexible film.

The modified collagen was then used to attach two sections of porous paper. The bond was strong and required significant force to separate the two sections. This same material was used to attach two sections of calf skin. UV irradiation in the absence of oxygen, was used as the initiator in place of the sodium persulfate. After 20 minutes, the sections were firmly attached.

In still another case, an aliquot of epoxy-collagen was added to two sections of porous paper and placed in the laminar flow hood for 10 minutes. The material polymerized and dried to a firm and extremely flexible film that bonded the two sections of paper.

EXAMPLE 6

METHACRYLIC COLLAGEN ADHESIVE AND TESTING

In this example, 200 ml of soluble collagen was modified at pH 9.0 with 30mg of methacrylic anhydride. The reaction continued for 30 minutes after which 10 mg of glutaric anhydride was added and reacted for another 30 minutes. The modified collagen was precipitated by adjusting the pH to 4.5. The precipitate was recovered by centrifugation and washed three times with sterile water. The material was reconstituted in 0.005M phosphate buffer containing 2% glycerol. The solution was clear and viscous. An aliquot was removed and exposed to 254nm UV irradiation. After 2 minutes, the material had formed a clear, firm film. Another aliquot was removed and placed on a microscope slide. After 30 minutes, the material had polymerized spontaneously to form a clear, firm film. Two sections of alcohol washed calf skin were placed on a microscope slide, and the interface coated with methacrylic collagen. After 16 hours, the sections were firmly attached. This sample was then incubated in sterile buffer at room temperature. After one week, the sections remained firmly attached.

EXAMPLE 7

HUMAN TISSUE ADHESIVE MATERIAL

In this example, human dermis was dissected from full thickness skin specimen and blended using an OMNI homogenizer with a Macro generator (10mm). The tissue did not pulverize in buffer or saline. To the tissue was added 5 mg of methacrylic anhydride per 200 mg of tissue. The tissue immediately pulverized to a fine suspension. A second aliquot of methacrylic anhydride was added to further solubilize the tissue. The pulverized tissue was centrifuged to separate the soluble frac-

tion from the dispersed fraction. The modified tissue in the soluble fraction was recovered by adding 3 volumes of 70% ethanol. The collagen immediately formed fibers. These were recovered by centrifugation and dried in a laminar flow hood. The dried material was then reconstituted in 0.005M phosphate buffer, pH 8.5, containing 2% glycerol. The thick solution was slightly cloudy and viscous. This chemically modified tissue (methacrylic) was exposed to 254nm UV light for 2 minutes to form a strong, flexible film which could potentially be used as an adhesive to bond tissue.

In another experiment, human tissue was treated with glutaric anhydride instead of methacrylic anhydride. Two aliquots of glutaric anhydride (15mg/200mg tissue) were used to disperse and solubilize the human tissue. The soluble fraction was isolated and reconstituted in buffer, as above. The viscous material was extremely sticky. One aliquot was placed on a microscope slide cover slip. After drying the droplets could not be removed from the cover slip, even with a razor blade.

What is claimed is:

1. A method for bonding soft tissues comprising the steps of:

applying a polymerizable collagen composition onto at least a portion of a surface of at least one of a first tissue and a second tissue;

exposing said polymerizable collagen composition to an initiator so as to initiate polymerization of said polymerizable collagen composition; and contacting said first tissue and said second tissue, wherein said exposed polymerizable collagen composition forms a bond between said first tissue and said second tissue.

2. The method according to claim 1, wherein the collagen is at least one member selected from the group consisting of purified Type I collagen, purified Type III collagen, purified Type IV collagen and collagen rich tissue.

3. The method according to claim 2, wherein the Type I collagen is derived from human tissue or animal tissue.

4. The method according to claim 3, wherein the Type I collagen comprises autogenic human tissue,

5. The method according to claim 1, wherein the polymerizable collagen comprises a reaction product of collagen with at least acylating agent selected from the group consisting of glutaric anhydride, succinic anhydride, lauric anhydride, diglycolic anhydride, methyl succinic anhydride, methyl glutaric anhydride, dimethyl glutaric anhydride, exo-3,6-epoxy-1,2,3,4-tetrahydrophthalic anhydride, 3,6-endo-3-methyl hexahydrophthalic anhydride, endo-3,6-dimethyl-3,6-endo-hexahydrophthalic anhydride, methacrylic anhydride, succinyl chloride, glutaryl chloride, and lauryl chloride.

6. The method according to claim 5, wherein the acylating agent is glutaric anhydride.

7. The method according to claim 5, wherein the acylating agent is methacrylic anhydride.

8. The method according to claim 5, wherein the acylating agent is exo-3,6-epoxy-1,2,3,4-tetrahydrophthalic anhydride.

9. The method according to claim 1, wherein the polymerizable collagen comprises a reaction product of collagen with at least one sulfonating agent selected from the group consisting of anthraquinone-1,5-disul-